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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,624	03/28/2002	Ikuro Maruyama	0760-0298P	8158
2292	7590	11/02/2004	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			LUKTON, DAVID	
			ART UNIT	PAPER NUMBER

1653

DATE MAILED: 11/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/980,624	<b>Applicant(s)</b> MARUYAMA ET AL.	
	<b>Examiner</b> David Lukton	<b>Art Unit</b> 1653	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 August 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) 2-6, 9-12, 14-17 and 20-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 7, 8, 13 and 19 is/are rejected.
- 7) ☒ Claim(s) 18 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Pursuant to the response filed 7/8/04, applicants elected Group 1 (claims 1-14, 17-19).

Applicants also attempted at that point to comply with the "election of species requirement" by electing the following:

- the adsorbent comprises a water-insoluble carrier on which a substance having sulfate groups is immobilized;
- cyanogen bromide provides the means of bonding the sulfate to the carrier;
- the sulfate is directly linked to the carrier, without the presence of a linker.

Subsequently, in the response filed 8/16/04, applicants elected the following:

- the adsorbent is in the form of beads;
- the "water insoluble carrier" is cellulose;
- the specific "substance" that is immobilized on the adsorbent is dextran sulfate.

Applicants have traversed the restriction requirement by arguing PCT rules confer

"immunity" from restriction. Consider, however, the following passage from the

MPEP (section 1850):

PCT Rule 13.2, as it was modified effective 01 July 1992, no longer specifies the combinations of categories of invention which are considered to have unity of invention. Those categories, which now appear as a part of Annex B to the Administrative Instructions, has been substituted with a statement describing the method for determining whether the requirement of unity of invention is satisfied.

Unity of invention exists only when there is a technical relationship among the claimed

inventions involving one or more special technical features. The term "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art.

The determination is made based on the contents of the claims as interpreted in light of the description and drawings. Annex B also contains examples concerning unity of invention.

**Independent and Dependent Claims.**

Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. By "dependent" claim is meant a claim which contains all the features of another claim and is in the same category of claim as that other claim (the expression "category of claim" referring to the classification of claims according to the subject matter of the invention claimed for example, product, process, use or apparatus or means, etc.).

If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention. Equally, no problem arises in the case of a genus/species situation where the genus claim avoids the prior art. Moreover, no problem arises in the case of a combination/subcombination situation where the subcombination claim avoids the prior art and the combination claim includes all the features of the subcombination.

If, however, an independent claim does not avoid the prior art, then the question whether there is still an inventive link between all the claims dependent on that claim needs to be carefully considered. If there is no link remaining, an objection of lack of unity (that is, arising only after assessment of the prior art) may be raised. Similar considerations apply in the case of a genus/species or combination/subcombination situation.

As it happens, claim 1 is far removed from any genus that is novel. Methods of ion-exchange chromatography (e.g., carboxymethyl cellulose and DEAE sephadex) were established more than 50 years ago; many such references would anticipate claim 1 or render it obvious. Subsequent to the early work on ion exchange chromatography, there has been a "mushrooming" of the literature on chromatography, including methods for cation exchange, anion exchange, hydrophobic interaction, affinity and even size exclusion chromatography, all of which are encompassed by claim 1 (at least the matrices

*per se*). To search for and reject over each of the many thousands of references that are applicable would constitute an "undue burden" by itself. But in addition, claim 1 does not "define a contribution" over the prior art. Accordingly, "unity of invention" is lacking. Notwithstanding the foregoing, however, in the event that claims within Group 1 are found allowable, methods of using the allowable adsorbents for adsorbing HMG proteins (or another purpose) will be rejoined for further examination. In addition, in the event that claims within Group 1 are found allowable, the possibility of rejoining claims 20-22 will be considered.

Pursuant to the restriction, claims 15, 16, 20-27 are withdrawn from consideration. In addition, claims 2-6, 9-12, 14, 17 are withdrawn, since they do not encompass the elected "adsorbent". Applicants have argued (response filed 7/8/04) that claims 14 and 17 encompass the elected species, but clearly this is not the case. Claims 1, 7, 8, 13, 18, 19 are examined in this Office action.



Claim 19 is rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 is dependent on claim 15, which describes a non-elected invention.



Claim 19 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP 608.01(n).



The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 19 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 19 asserts that a water-insoluble matrix bearing amino groups or carboxyl groups or sulfate groups can somehow be used to treat sepsis. However, there is no reason given for why the skilled artisan would believe this to be true. Certainly there is no literature to support such an assertion; there are no examples in the specification to support this. And even if the claims required the presence of antibodies to HMG proteins, there would still be no reason to expect therapeutic efficacy.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400,

Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. The state of the art is such that the skilled artisan would have expected failure in the treatment of sepsis using, e.g., carboxymethyl sephadex, or diethylaminoethyl sepharose, whether or not antibodies were present. Given the absence of guidance, the absence of working examples, and the unpredictability of the art, "undue experimentation" would be required to practice the invention of claim 19.



The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not

commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 7, 8, 13 and 19 are rejected under 35 U.S.C. §103 as being unpatentable over Stuber (USP 5,116,962).

Stuber discloses an adsorbent bearing sulfate groups. Stuber does not disclose that the adsorbent will adsorb HMG proteins. However, the chromatographic specialist (of ordinary skill) would have expected that if the pH of the eluting buffer is below the isoelectric point (IEP) of a given protein, there will be at least some adsorption. That is, if one were to take a given protein "X" which has an IEP of "Y", and load that protein "X" onto a sulfated chromatographic matrix, the result would be that protein "X" would elute after the void volume if the pH of the buffer were less than the IEP.

Thus, the claims are rendered obvious.



Claims 1 and 19 are rejected under 35 U.S.C. §103 as being unpatentable over Abbot (USP 4,430,496).

Abbot discloses an adsorbent bearing trimethylammonium groups. Abbot does not disclose that the adsorbent will adsorb HMG proteins. However, the chromatographic specialist (of ordinary skill) would have expected that if the pH of the eluting buffer is above the isoelectric point (IEP) of a given protein, there will be at least some adsorption. That is, if



one were to take a given protein "X" which has an IEP of "Y", and load that protein "X" onto a cationic chromatographic matrix, the result would be that protein "X" would clute after the void volume if the pH of the buffer were above the IEP of the protein.

Thus, the claims are rendered obvious.

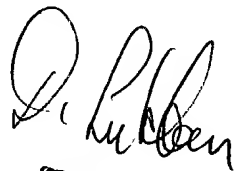
\*

No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached at 571-272-0925. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

  
DAVID LUKTON  
PATENT EXAMINER  
GROUP 1500